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Prepared by

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The paper suggest a mechanism for the inactivation of kinins and angiotensins in the brush border of the nephron.

METABOLISM OF KININS AND ANGIOTENSINS IN THE KIDNEY

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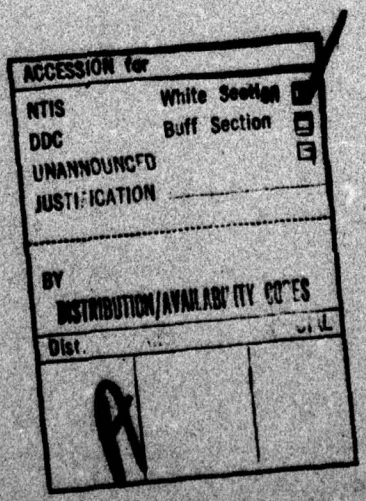

The kidney is rich in the enzymes which form or inactivate kinins and angiotensins. These vasoactive peptides have potent effects on renal blood flow, salt-water balance and prostaglandin release. If intrarenal generations of these peptides are physiologically significant modifiers of renal function, their rates of inactivation are equally important.

The kidney has a very high kininase content (1). In the homogenized kidney most of this activity sediments with the microsomal fraction. Erdös and Yang (2) described several of these renal kininases. One of them is a carboxypeptidase (kininase I) while the other (kininase II) is identical with the angiotensin I converting enzyme (3,4).

Kinins (5) and angiotensins as well (6), are rapidly and nearly completely inactivated when infused into the kidney. Little or no intact bradykinin reaches the venous effluent or urine. Urine does, however, contain kinins (7), which are apparently released intrarenally.

Unlike renal kallikrein which is localized primarily in the cortex (8), renal kininase and converting enzyme are present in both cortex and outer medulla (9). After fractionation of renal microsomes into plasma membrane and endoplasmic reticulum-enriched fractions, renal kininase, converting enzyme (10) and angiotensinase, (possibly A type), were found predominantly in an enriched fraction of plasma membrane (11,12). Isolated brush borders of proximal tubules (Fig. 1) are particularly rich in these enzymes while little activity was found in isolated glomeruli (12,13). Transplanted renal tumors, thought to be derived from cells of the pars recta of proximal tubules, also contain kininase, converting enzyme and angiotensinase (12,14). In contrast, kallikrein was not present in the brush border of proximal tubules because it originates from distal tubules.

Another approach to show kininase II in the kidney consisted of using fluorescent antibody to purified swine kidney enzyme. By this technique converting

enzyme was found throughout the nephron, but more concentrated in the proximal tubule (14) than in the distal tubule (Fig. 2). In rabbits (15) converting enzyme is also present in the proximal tubules. Both studies reported much lower levels associated with the glomerular tufts (14, 15).

Using micropuncture of proximal and distal tubules, Carone et al. (16) and Pullman et al. (17) have shown that the proximal tubule is highly active in hydrolyzing added bradykinin and angiotensin II. Little or no activity was found in the distal tubule.

After considering all of these observations, we suggest the following mechanism for renal inactivation of kinins and angiotensins (Fig. 3). If kinins and angiotensins released intrarenally have important effects on water and sodium metabolism and prostaglandin release, the kidney must be capable of inactivating these peptides entering the nephron from extra-renal sources. The low molecular weight of these peptides makes it likely that any plasma kinin or angiotensin that escapes inactivation in the circulation is filtered at the glomerulus. High levels of kininase and angiotensinase on the huge surface of the brush border of the proximal tubules then ensure complete removal of these peptides from the tubular filtrate which eventually reaches the distal tubules. At the distal tubule, renal kallikrein (11,12,18) interacts with a plasma or tissue kininogen to release renal kinin. The level of kinin at this site can be closely controlled since all traces of extra-renal kinin have been removed. Kallikrein by liberation of (19), renal kinin (20) may alter ion transport, water reabsorption and liberate prostaglandins (21) in collecting tubules and ducts.

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Legends

Fig. 1. Scanning electron micrograph of brush border of proximal tubules in rat kidney (12).

Fig. 2 Fluorescent photomicrography (X90) of a 4 μm section of swine kidney cortex incubated with fluorescein isothiocyanate labeled antibody against angiotensin I converting enzyme (14).

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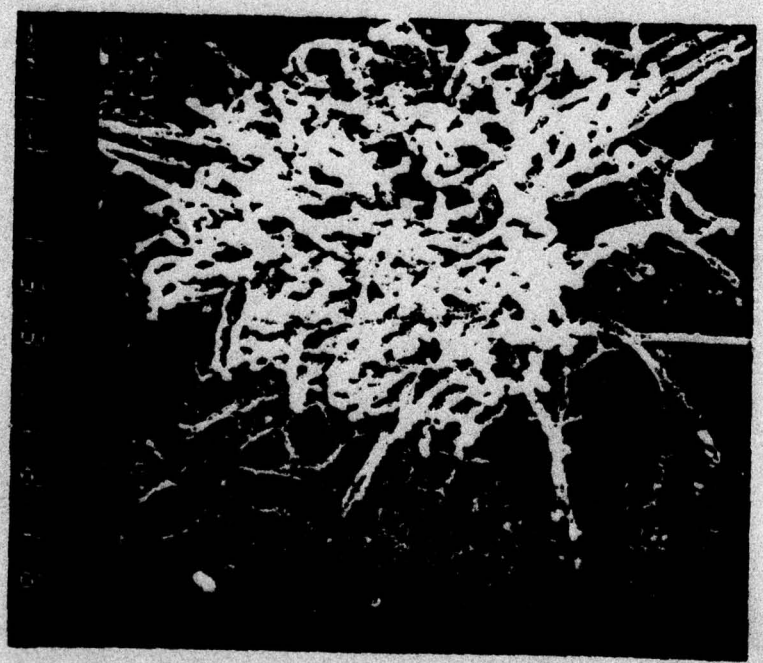

RENAL METABOLISM OF KININS & ANGIOTENSINS

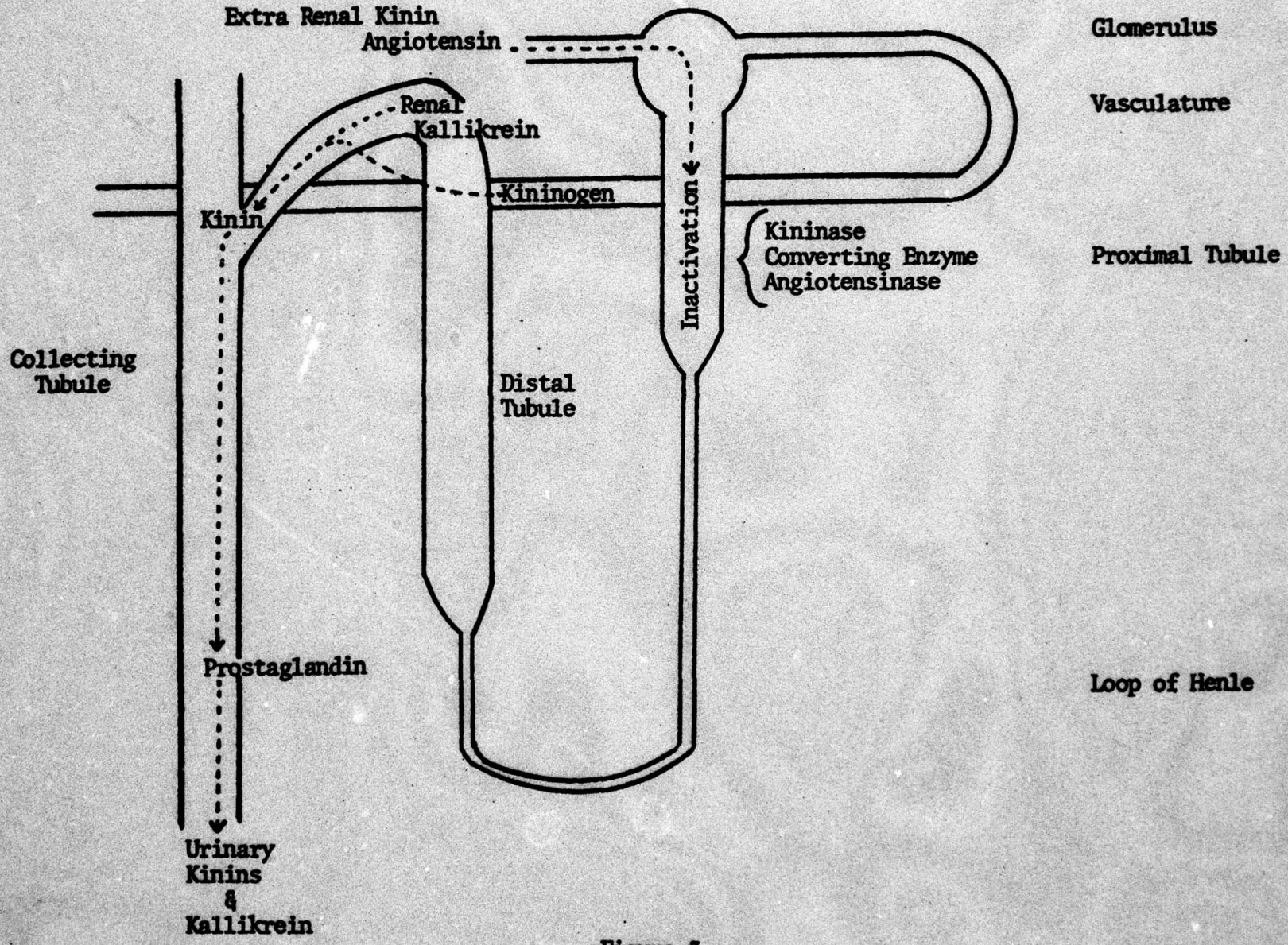

Figure 3